



Second Opinion

Second opinion

Little Red Riding Hood and the Wolf

The article in the Times made Second Opinion feel distinctly nostalgic. Even in the kindergartens of our country the splendid old nursery games are being replaced by the invading computer. No longer apparently does one hear the cries of 'Oranges and Lemons' followed by a spot of execution or the sounds of 'Ring a Ring of Roses' but instead there is the monotonous bleep of the computer game. A sad and sorry state of affairs when Peter Rabbit has just clocked up his centenary. Mind you, even if the nursery rhymes are taking a bit of a knocking in the school playground the nursery stories cannot be avoided in the large Victorian institution in which Second Opinion has been condemned to spend his days. Rescued from the demolished Victorian childrens Ward, Doulton murals continue to gaze down from the walls of corridors and lobbys. From time to time one sees small knots of elderly adults gazing up at them, visitors on special trips to admire 'Little Boy Blue', 'Hey Diddle Diddle' are sunk into the subconscious by doting parents. The stories of the cot seem so cosy but have you ever noticed their underlying streak of violence. The execution in 'Oranges and Lemons' is presumably a reference to comings and goings at Tower Hill. The Wolf of 'Little Red Riding Hood' - what a nasty character and then there is the origin of Ring a Ring of Roses.

b) For real knowledge who were the Dish and the spoon in Hey Diddle Diddle?

Now you may well be wondering why you have been affected by such a ridiculous beginning to this problem solving exercise. However, to let you into a secret, Second Opinion had been reflecting on the splendid series of Doulton tiles that depict the story of Little Red Riding Hood. There is the little girl in the forest all dressed up with cloak and bonnet. The horrible, horrible wolf masquerading as the recently consumed grandmother and of course the good hunter riding to the rescue. An analogy of medical practice perhaps. Death, disease and doctor surrounding a little patient. Try this one.

The child was a little older than Red Riding Hood and was of the opposite sex. A sparkling vivacious 11-year-old with fair hair and blue eyes. The very apple of his parents eye, he was an only son and his parents had waited a long time for him. In fact his mother was in her early 40s when he was born. He was worth waiting for. Good at games, good at work and together with his extroverted personality he seemed to have been given more than his fair share of talent. His problem appeared simple, merely swelling and discomfort in his right ring finger. He had knocked this finger whilst playing in the school playground with his friends a few weeks before. At the time the injury did not seem particularly severe as it had merely been struck and hyperextended by a football. However, the next day it was clearly bruised and swollen so his mother took him to the local GP. He was not particularly interested. He knew the family well. Being an only child mother tended to fuss and there had actually been numerous attendances at the GP's surgery though the child had never had a single day's serious illness in his life.

The discomfort in the finger settled spontaneously

Questions

Question 1

- a) For general knowledge what is the origin and meaning of the Nursery Rhyme Ring a Ring of Roses?
Why 'atishoo, atishoo'?
Why do we all fall down dead?



Fig. 1

but the swelling did not. Movements were slightly restricted but not to the extent that it interfered with normal function. That is how the situation remained for the next 3 months. Mother, although she remained concerned about the swelling, was reluctant to return to the GP having had rather short shrift on the first occasion. However, at the end of the 3 months the finger again became painful. This time there was no history of injury. The GP was surprised to see the child again and even more surprised to see that the finger was still swollen. He wondered whether he had missed an undisplaced fracture. The swelling was most marked over the proximal phalanx and faded out to normal more distally. In this respect the finger was slightly conical. Apart from the swelling the alignment was good and there was surprisingly little loss of mobility considering the extent of the swelling. On flexion the finger came down to within half an inch of the palm. In view of his thought about a fracture the GP arranged for an X-ray. This was duly done and is shown in Figure 1, July 1984.

Question 2

Your thoughts on the X-ray. What do you observe and what is your diagnosis?

The GP received the report but not, of course, the X-rays. He sent for the child plus the mother and informed them that there was chronic infection in the bone. He took some blood for a white count and ESR both of which were later reported as normal. He took the child's temperature which was also normal and prescribed a course of antibiotics, in fact he gave the child penicillin. On review a week later the GP was very pleased to find that the symptoms had settled

within 48 h of being given the penicillin and that the tenderness had settled. The swelling seemed slightly less but the finger was still quite thickened. In view of the good response and other normal investigations the GP decided to do nothing more except to observe the finger for the next few weeks. In essence nothing changed during this time and the GP decided to take no further action.

One would not want to ask you whether this was a wise or correct course of action but one must remember that the GP, to do him justice, only had the radiologist report, he did not actually have the films. Since we have the benefit of seeing the films one hopes that you the reader will be a little surprised that the finger responded so satisfactorily to penicillin. Needless to say the story continued. Indeed if it had not one would not only have been surprised but one could not actually construct a Second Opinion! 3 months later, the same time interval as on the previous occasion, the finger again became painful. Once more there was a dubious history of it being knocked in the playground. The child himself seemed otherwise well. On this occasion the GP remembered to examine the axilla for any lymph nodes (it is hoped that the reader did this on the first occasion!). There was no local adenopathy. The child was again given a course of penicillin. The response to treatment was not as dramatic as on the first occasion but nonetheless over the course of the next week the finger did improve. However, as it was still slightly tender the GP thought it was time to get a specialist opinion. He rang the local hospital and spoke to the Registrar who said that he would see the patient at the end of the clinic the following morning.

The Registrar was not exactly on the best form the next day. He had been on duty during the night and had spent most of it in theatre dealing with a multiple injury. To be truthful he was not best pleased when, after struggling to the end of the clinic, he was told by Sister that he still had to see a child with a swollen finger. The Registrar had actually forgotten about his conversation with the GP the day before.

The GP had written a good letter of referral which outlined the previous history. He also enclosed the radiologists report but unfortunately, since no-one had read the letter prior to the patient reaching the Registrar, the X-ray was still in filing. He saw the child and observed the same signs as the GP, namely a swollen finger, a slight residual tenderness, not much in the way of any actual signs of redness or inflammation, and an almost full range of movement in the metacarpo-phalangeal and interphalangeal joints. Clinically he thought that this was compatible with a resolving episode of chronic infection. He added Fucidin to the penicillin and arranged for a follow-up appointment in 2 weeks time. It was now past lunchtime and the Registrar retired somewhat wearily for something to eat. It was meant to be his research afternoon but his brain was functioning none too well so he went home, went to sleep and he forgot all about seeing the X-ray. 2 weeks later he had a



Fig. 2

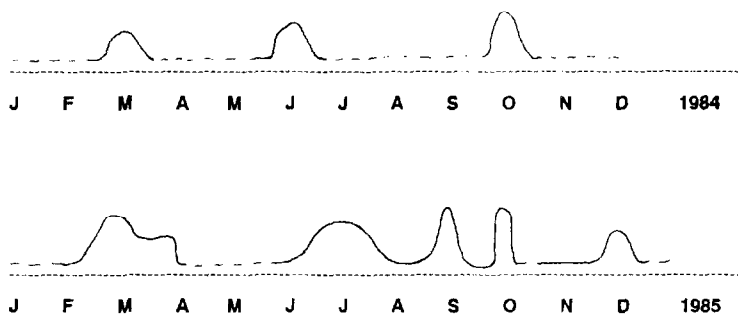
nasty surprise As the child and his mother walked into the consulting rooms Sister put up the X-ray on the viewing box. The Registrar could scarcely believe his eyes for it looked awful. He turned hurriedly to the back of the notes for the blood investigations and was relieved to find that the ESR was normal as was the white count and Hb. He looked at the child's finger and was somewhat relieved to find that there was no longer any residual tenderness. It had clearly responded to the antibiotics. He took the child along the corridor to show him to his Consultant. The first thing the Consultant wanted was the recent X-ray and the Registrar somewhat shamefacedly had to admit that in his alarm at seeing the X-ray he had quite forgotten that it was 3 months out of data.

Question 3

What would you now advise? The 'new' X-ray dated October 1984 is shown on Figure 2.

The Registrar duly explored the finger the following day approaching the proximal phalanx through a mid-lateral incision. The soft tissues were slightly oedematous in keeping with the soft tissue swelling. Somewhat to his surprise, however, the bone seemed grossly normal. He took two small specimens, one for histology and one for culture. Incidentally, if you did not remember to send the specimens for histology and for culture you would probably be lost without trace if you were in an exam! Nothing was grown on culture. The Registrar was not at all surprised when a couple of weeks later he got the following histology report 'A single small fragment of bone with intertrabecular tissue. There is no evidence of any inflammation and no tumour cells are seen'.

The Registrar discussed the case again with his Consultant and they decided the best plan of action was to do nothing in particular but to continue to observe the child who was asked to attend for monthly appointments. For the next 3 months everything was satisfactory and the only sign of any problem was that the finger remained slightly swollen. Once again there was then a rather dubious history of minor trauma following which the finger became painful, tender and slightly more swollen. A further course of penicillin and fucidin was given and once again the inflammation settled. The chart in Figure 3 outlines the sequence of the recurrent attacks in 1984 and 1985. On each occasion the child was given a further course of antibiotics, usually fucidin and penicillin. These seemed rather less effective than they had been in treating the two attacks that occurred in 1984. At no stage was there any pyrexia and the ESR and white count which were repeated on several occasions remained obstinately normal. As you will observe in the Autumn of 1985 there were two attacks relatively close together in September and October and as a result the case was discussed at the local orthopaedic conference. The X-ray taken on 1 October 1985 is shown in Figure 4. The Consultant in charge of the case, incidentally was the youngest member of the staff and he had only been in post for 3 or 4 years. He was particularly interested to get the opinion of his senior colleague whom he much respected when it came to old fashioned diseases.



(This is not a temperature chart!)

Fig. 3—A diagram to illustrate the occurrence of a 'flares' during 1984 and 1985.

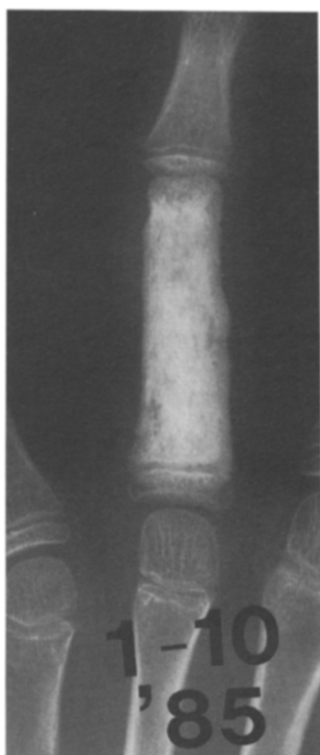


Fig. 4

Question 4

What do you suppose the conference concluded and what plan of action was advised?

By now the original Registrar had rotated to another post in another hospital. A new, recently promoted, Senior Registrar carried out the exploration. He too was surprised at the relative normality of the bone. He took a rather larger biopsy than on the first occasion and was relieved to find that when he went deeper into the bone it did not seem quite so normal. It appeared as if it had an outer reactive shell. Once again the specimen was sent for both culture and histology. As will be seen from the symptom chart the finger settled quite quickly immediately following the biopsy but had a further flare in the following month. The child had actually been on penicillin and Fucidin since the second biopsy. The flare in November was in fact the first occasion on which the finger had flared whilst the child had been on antibiotics. Cultures of the biopsy were once again negative, including the long-term culture for tuberculosis. The histology of the second biopsy was reported as follows:

'Several fragments of bone and periosteal fibrous tissue. The biopsy shows marked crush artefact but in one section there is an aggregate of round cells in the periosteum which have the appearance of lymphocytes. The appearances are non-specific but could be compatible with a low grade chronic inflammation.'

Everyone was rather puzzled. 6 weeks had elapsed by the time all these investigations had been completed. No-one was quite sure what to do but fortunately the symptoms then settled and the only residual feature of the problem was that the finger remained swollen but no more swollen than it had

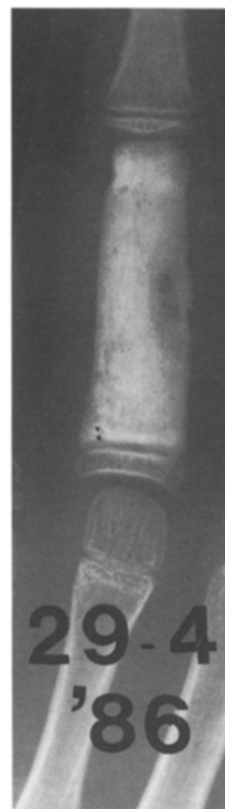


Fig. 5

been when the child first presented. For the next 6 or 7 months, until the Summer of 1986 the child remained well. An X-ray, Figure 5, taken at the end of April 1986 showed that there had been no significant change in the X-ray. The area of bone erosion which you can observe on Figure 5 is of course the site of the biopsy. Further pursuit of the diagnosis seemed entirely academic. The child was discharged from the clinic with the instruction to return should there be a further flare of pain.

Towards the end of May 1986 the story took an unexpected turn. The patient, who had just become a teenager, developed pain in the left groin. The GP examined the hip but could find no abnormality and in particular the range of movement was full. However, bearing in mind the saga of the finger he was not going to take any risks and duly dispatched the patient up for an X-ray. On this occasion he was relieved to get the X-ray report which said that the pelvis and hips were normal. However, when he saw the child again the following week the symptoms from the hip were, if anything, worse and the mother stated that her son had been limping towards the end of the day when he came home from school. The GP arranged for an urgent appointment to see the Consultant.

Question 5

Would you pass this X-ray as being normal? (Figure 6).

The Consultant saw the patient in the second week of June, i.e. a week after the X-ray shown in Figure 6. He agreed with the GP's findings. The hip was clinically normal with a full range of movement. In

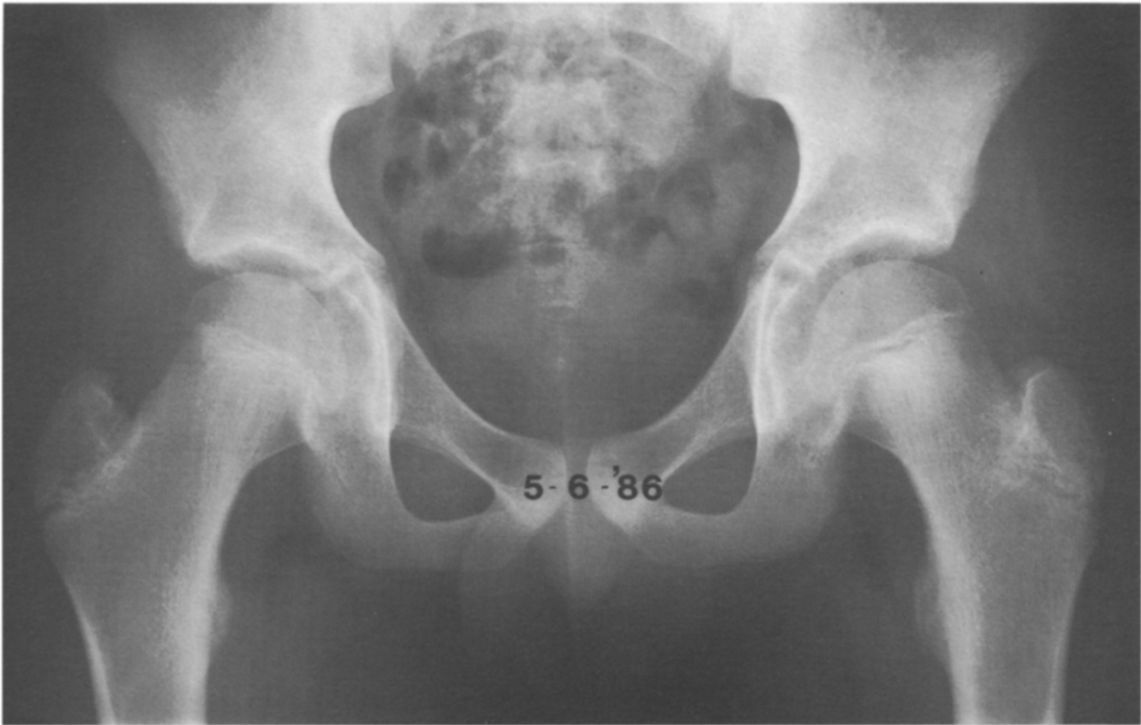


Fig. 6

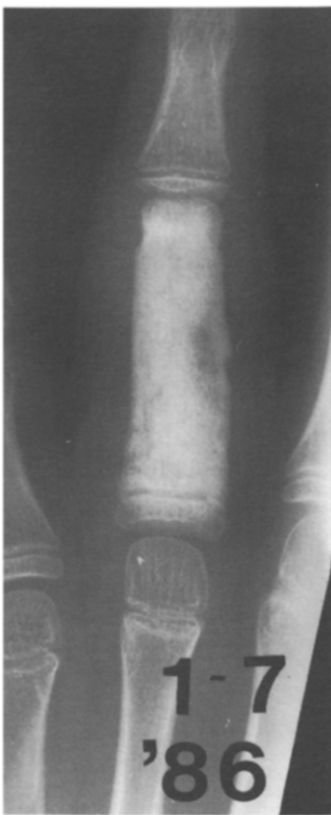


Fig. 7

particular the finger remained symptom free apart from its residual swelling. However, he did not like the look of the hip X-ray and arranged for a further attendance at the orthopaedic conference in a couple of weeks time. This took place on 1 July. A further X-ray of the finger was taken specifically for this visit and is shown in Figure 7. Conference thought that the

finger and also its X-ray had shown some improvement with a gradual healing in of the biopsy site. There was much discussion about metastatic infection from rare organisms. The Senior Registrar who was very much on the ball asked 'could this be actinomycosis?'. A debate ensued as to whether or not the hip should be biopsied. It was felt that the lesion was very close to the epiphysis and hence there was a danger of interfering with growth. The decision was taken to give a further course of penicillin and fucidin but to do a biopsy if the symptoms did not resolve. The Senior Registrar incidentally thought that this advice was a typical committee decision and could see no logic in it. Having been dissuaded out of his idea of actinomycosis, he agreed the most likely cause was tuberculosis. He felt with considerable justification that his senior colleagues would have more than a little difficulty with the examiners if they avoided making a definitive bacteriological diagnosis. (He was quite correct. They would fail! Second Opinion hopes you were not lulled into this error. The Senior Registrar was incidentally due to sit his Board exams in November that year. He looks like a pass!) He felt that the response to antibiotics in the past may have been entirely spurious since one could equally argue that the episodes of pain in the finger merely waxed and waned from time to time, i.e. the disease being episodic any form of treatment given at the right moment would be bound to be effective. If one was going to give antibiotics one would give a proper course of antituberculous treatment. His argument did not prevail.

Not only did the fucidin and penicillin make no difference to the hip pain but a week later the finger again flared. As regards the hip the symptoms took a

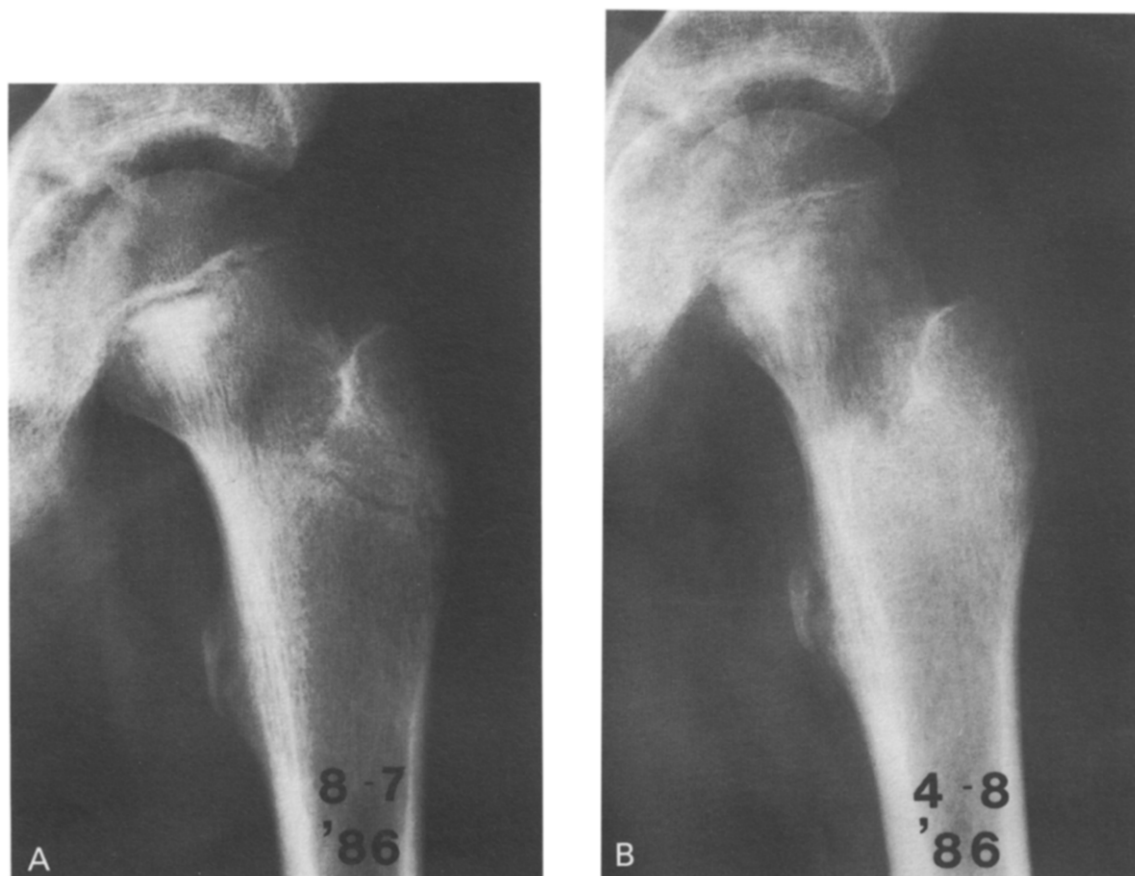


Fig. 8

sudden turn for the worse over one weekend at the end of July. He was again seen in a clinic the following week and it was now evident that he could not take any weight on this left leg without limping badly. A further X-ray was taken.

Question 6

Figure 8 shows two AP X-rays one taken on 8 July and the other on 2 August. Once again your thoughts please.

The Consultant was alarmed by this X-ray and immediately admitted the boy with a view to exploring the hip. The Consultant did this himself the following day. He made a drill hole in the lateral cortex just below the greater trochanter and used a curette to remove some bone from the neck of the femur. The curettings did not seem particularly abnormal though the bone was rather soft. He had expected to find some pus present but none appeared. The curettings were sent for histology and culture in the standard manner. Postoperatively the patient was put on skin traction and continued on bed rest.

The culture was again negative but the histology aroused considerable interest. The report read as follows:

'Some necrotic bone and fibrous tissue. There are two small areas of lymphocytic infiltration. The specimen is of rather poor quality due to the surgical disruption but the appearances are not diagnostic'.

Everyone was well and truly puzzled. The only slight advance that they had managed to make was that the presence of lymphocytes, albeit in small numbers, had been noted in both the biopsy of the finger and of the hip. It seemed likely that they were dealing with the one disease but apart from this nobody was any the wiser. All sorts of people were asked to see the patient including the paediatricians, the microbiologists and even a radiologist. In desperation the boy was put on a course of anti-tuberculous treatment. However, during the month of August his symptoms did not improve. Indeed they became gradually worse and the hip which a few weeks before had a normal range of movement became irritable. A further X-ray taken on 4 September (Fig. 9) showed a dramatic change for the worse. There was still an area of sclerosis near the epiphysis but the epiphyseal plate itself seemed to be disappearing as indeed did part of the neck. Some callus had appeared just above the lesser trochanter and it seemed that a pathological fracture may be imminent. In view of these changes a further exploration of the hip was carried out. On this occasion much to the surgeons relief pus was obtained. There was a small amount lying deep to the fascia lata and this seemed to extend up the previous drill hole through the lateral cortex of the femur. Macroscopically there seemed to be some small occlusion bodies in the tissue that was sent to the laboratory labelled 'pus'. The Senior Registrar cried 'Eureka.



Fig. 9

sulphur granules'. The specimen of pus was conveyed in triumph to the Microbiology Department who were asked to culture it for both aerobic and anaerobic organisms and for that matter anything else that the microbiologists could dream up! Further curettings were taken from the neck of the femur and sent for histology.

The triumph of the surgeon in finding pus was short lived for the microbiologist failed to culture anything. The histology report, however, was more interesting. This showed that there was extensive bone necrosis. Indeed so much so that the specimen was difficult to interpret. There were some areas of haemorrhage and on one of the curettings some new bone formation. In comparison to the previous biopsy more lymphocytes were present. No hyphae were seen.

Question 7

What do sulphur granules imply?

Unfortunately the SR had to admit that there was nothing to support the diagnosis of actinomycosis. Indeed it seemed to him that they were still without a diagnosis. A battery of blood investigations failed to be of any help. It is true that his ESR had risen to 25 mm/h but this was hardly dramatic considering the fact that the boy had now had two biopsies of his hip. Sadly over the next 2 weeks the patient's symptoms became much more severe and the hip drifted into a

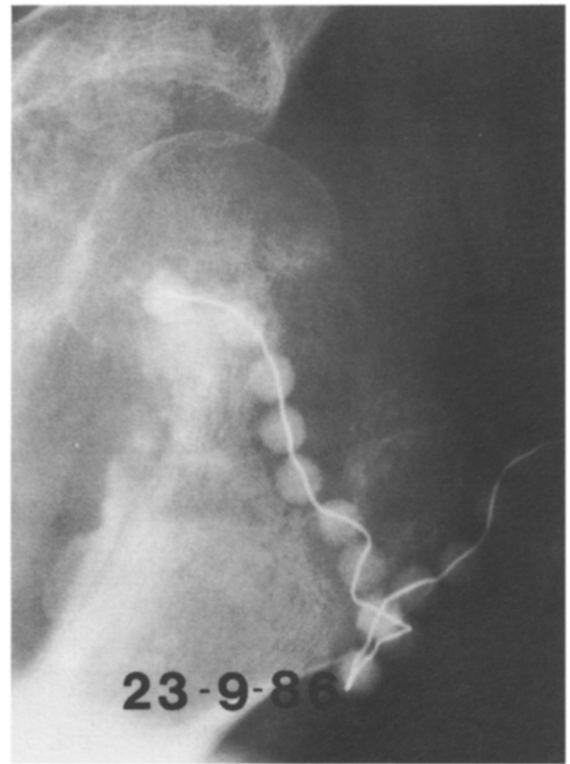


Fig. 10

position of marked adduction. The leg was excruciatingly painful to even rotate and the nurses had considerable difficulty in nursing him. In mid-September the wound on the thigh became progressively more and more inflamed. The thigh itself developed a fullness extending right round over the groin and the leg itself became oedematous. An X-ray showed that the hip was beginning to sublux. The Consultant felt absolutely certain that this was an infection in which they had failed to grow the organism. He, therefore, undertook a further exploration on 23 September 1986. As can be seen in Figure 10 this time he left nothing to chance and even put some gentamycin beads up into the femoral neck. The curettings, however, on this occasion produced in addition to a considerable amount of rather necrotic looking tissue some fleshy masses of soft material.

Question 8

It is time for a proper diagnosis! What is the matter with this boy?

A knowledge check. In order to assist your revision, Answer the following questions about Ewings:

1. The age distribution
2. The sex distribution
3. The skeletal distribution
4. List the prognostic factors
5. What are the radiological appearances and what is the reason for their variability?
6. Is there anything special to note about doing the biopsy?

7. How is it treated?

8. What are the results of treatment?

An excellent review article on Ewings was published in *Clinical Orthopaedics and Related Research* in January 1991 by O'Connor and Pritchard. This is certainly worth reading. An excellent article on the plain X-ray appearances of Ewings was published as long ago as 1967 by Vohra who examined 156 cases. This article clearly illustrates the variation in the plain X-rays and underlines the ability of Ewings to deceive.

As a brief summary of the above questions: approximately 40% of cases will present between 10 and 20 years old, 25% below 10 and 25% between 20 and 30. A very small number may occur in middle age and it has not been unknown in patients in their 50s. The sex distribution is a male abundance by 2:1. The commonest site is the long bones, particularly the femur but the pelvis, ribs and scapula are other favoured sites. It has been reported in a wide variety of bones but it is very rare in the hand. Lacey et al in a single case report on a Ewings of a proximal phalanx of the finger could find only 13 other cases in the literature. 9 of these involved the metacarpal, 3 the proximal phalanx and one the distal phalanx. The case reported in this second opinion is therefore extremely rare, nonetheless it illustrates all the pitfalls about Ewings.

As regards risk factors the following have a worse prognosis: pelvic lesions, tumour volume of over 100 ml, tumour size of over 8 cm, age—the younger do better, raised sedimentation rate and raised white count. The reason for the radiological variability is in essence due to the site of the tumour within the bone. The variation is enormous from superficial erosions to extensive sclerosis. The latter in particular tend to get mistaken for chronic infections as in this case and the real error here was of course not to pursue the diagnosis. This was not helped by the first biopsy of the finger being only of the outer cortex! As regards treatment multiagent systemic chemotherapy plus radiotherapy have been the cornerstones of treatment but surgery seems to be making a comeback. It is particularly useful in dealing with bones that can be easily sacrificed, for instance a finger. This is well dealt with in the article by O'Connor and Pritchard. The 5 year survival rates now range from approximately 55% to 75% for patients with localised osseous Ewing's sarcoma.

Answers

Answer 1

- a) This nursery rhyme of course refers to the Great Plague. The Ring of Roses was the skin rash, the atishoo was the pneumonia and death was inevitable.
- b) Hey Diddle Diddle refers to comings and goings in

the Palace. The Dish and the Spoon are the Prince Regent and Mrs Herbert. The comings and goings don't change too much over the years?

Answer 2

The GP was sent the following report from the Radiologist 'There is marked sclerosis and uniform thickening of the proximal phalanx of the finger involving all the bone except for the epiphysis at its base. These findings would be compatible with chronic infection.

Answer 3

The Consultant told the Registrar to do an urgent biopsy. The Consultant thought that the most likely diagnosis was indeed a chronic infection as the child had responded to two courses of antibiotics. However, he was only too well aware that no-one knew the organism. How would you do this biopsy and what investigations would you request?

Answer 4

Conference concluded that much of the most likely diagnosis was a tuberculous dactylitis. They advised that the child should have a Mantoux or equivalent test and that if this was negative a further biopsy should be carried out. The senior Consultant had been most surprised by the operative findings and the histology. He just wondered whether the biopsy had not gone deep enough.

Answer 5

There is an area of sclerosis in the metaphysis immediately adjacent to the epiphysis of the left hip. (Second Opinion hopes that this shows adequately when the AP of the pelvis is printed.)

Answer 6

Second opinion very much hopes that you did not pass these X-rays as normal? You might be excused for missing the area of sclerosis in the June X-ray but these films show a rapid progression of both the sclerosis and at the base of the neck an area of mottled osteoporosis indicating bone destruction. There is possibly some periosteal reaction on the medial border of the neck proximal to the lesser trochanter.

Answer 7

They imply actinomycosis. Without cheating by looking at the next paragraph in this answer just call to mind a few facts about actinomycosis.

Actinomycosis is due to an infection with the anaerobic fungus *actinomyces israeli*. This organism grows in tissues in the form of colonies composed of

mycelial threads with clubbed ends the so called ray fungus. Its colonies appear in pus as sulphur granules. At least 50% of the sites of infection are to be found in the cervico-facial area. These usually originate in the site of an injury in the jaw, for example a tooth socket. 25% of infections are in the abdomen usually presenting as an appendicular abscess. Pulmonary involvement occurs most commonly following aspiration or inhalation of the organisms. Acute disseminated infection is extremely rare and occurs where blood spread produces actinomycosis in many organisms. Characteristically the macroscopic lesion is that of a hard indurated swelling of the infected tissues which on cross section give the appearance of honey combed abscesses. Microscopically of course the appearances are made specific by the presence of colonies of the fungus together with a moderate polymorph infiltration and very extensive fibrosis. Diagnosis is obviously dependent on the identification of the organisms in the pus or in the tissue. The disease results in extensive tissue destruction and scarring but only occasionally is there a fatal outcome.

Answer 8

This is a Ewing's sarcoma. The child was referred to the regional centre. He was treated with chemotherapy and radiotherapy but sadly it was of no avail and he died a few months later. His elderly parents were heartbroken. This was not one of Second Opinion's own cases but as he returned from the library down the old Victorian corridor he passed the Doulton tiles. There was the wolf with gloating eyes, a greedy grin and ferocious teeth sitting dressed in grandmas hat and there was the child, but where was the doctor to rescue Little Red Riding Hood? Yes, several doctors had passed that way but none of them had had the knowledge.

A Ewing's sarcoma is not easy. It is usually far from classical in radiological appearance and it can be deceptive histologically. A review of the histology showed that the first finger biopsy in 1984 did indeed fail to reveal any tumour cells. The reason of course was that the biopsy was small. The Registrar had made the cardinal error of only biopsying the outer shell of cortical bone. This of course is merely reactive

to the underlying disease within the bone. The second biopsy was indeed difficult to interpret but the round cells were in fact not lymphocytes and were almost certainly tumour cells. The three femoral biopsies were all considered to show Ewing's sarcomatous cells. Characteristically Ewing's tumour cells lack clearly defined cell boundaries and their nuclei which can be round or ovoid are twice as great in diameter, or in the case of the ovoid ones possibly three times as great, as the nucleus of a lymphocyte. They have finely divided or chromatin and often one or more nucleoli. Obviously they should not be mistaken for lymphocytes but the actual field of cells is very variable and they can be mistaken for lymphocytes when the field is small. When the tumour becomes necrotic and liquifies then it can be mistaken for pus which is of course what happened with the second hip biopsy. It is easy to blame the histologist but the fault lies just as much, if not more so, with the surgeon who until the third biopsy was taken failed to produce an adequate specimen. In the first biopsy he may well have been afraid of damaging the epiphysis and hence was too timid. In the second biopsy he had heaved a sigh of relief when he had found some pus but in fact he had only largely obtained necrotic material and it was not until the third biopsy that he produced a good specimen.

Radiologically Ewing's is one of the 'jokers in the pack diseases'. The classical onion skinning periosteal reaction only occurs when the tumour is involving the diaphysis. Second Opinion sometimes thinks that it is the widespread knowledge about the onion skinning that easily lulls the unwary into a false sense of security as regards the ability to diagnose this tumour. We know this fact and we look for it. When it is not present Ewing's fails to register. Do not forget the old rule 'Infection limits movement. Tumours preserve movement'.

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